REMARKS

Claims 1-20 are pending. Applicant acknowledges the renumbering of the claims and has, accordingly, adopted the claim numbering proposed by the Examiner. Claims 3, 5-6, and 15-20 are canceled herein without prejudice. Claims 1, 2, 4, and 7-14 are amended herein to clarify the claimed subject matter. Accordingly, instant claims 1, 2, 4, and 7-14 are under consideration.

Support for amendment to the claims is found throughout the specification and in the original claims. Specifically, support for amendment to claim 1 is found in original claims 1, 5, and 6 and, for example, in the Abstract and Figure 1, and in paragraphs [0006], [0018], [0023], [0025], and [0049] of United States Published Patent Application Number 2006/0246449, which corresponds to the instant application. Support for amendment to claims 2, 4, and 7-14 is found in original claims 2, 4, and 7-14. Support for amendment to claim 14 is also found in paragraph [0006]. No issue of new matter is introduced by these amendments.

The Examiner's comments regarding certified copies of the priority documents are noted. Certified copies of the priority documents have been ordered and will be forwarded to the Examiner upon receipt.

Rejection under 35 USC § 112

Claims 1-20 have been rejected under 35 U.S.C. § 112, second paragraph, for allegedly indefiniteness for recitation of the phrase "the reference one or more SNPs" in claim 1 and phrases "the sequencing reaction(s)" and "detecting the incorporation of bases into the immobilized oligonucleotide to determine at least the unique coding sequence" in claim 6, which are viewed as lacking proper antecedent basis. Claim 1 is amended herein to clarify the claimed subject matter. Claim 6 is canceled herein, thereby obviating any rejection of this claim. Claim 14 is rejected for the limitations "5'-iodide and 3'-selenophosphate" which are allegedly unclear. Claim 14 is amended to clarify the metes and bounds of these limitations. In view of amendments to claims 1 and 14, the rejection, as it applied to claims 1-20, is respectfully traversed.

In view of the amendments to the claims, the Examiner is respectfully requested to reconsider the validity of the rejection of the claims under 35 U.S.C. §112 and withdraw the rejection.

Rejection Under 35 U.S.C. § 102

Claims 1-3, 8-12, and 15 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Landegren et al. [United States Patent Number (USPN) 4,988,617; 1991]. Claims 3 and 15 are canceled herein, thereby obviating any rejection of these claims. In view of the clarifying amendments to the claims and Applicant's arguments presented herein, the rejection as it applied to claims 1-3, 8-12, and 15 is respectfully traversed.

The instant claims are amended to clarify that the method calls for a unique label, which is a unique coding sequence of nucleotides that is specific for the nucleotide complementary to the known SNP site and the position of the SNP to be scored. In accordance with this feature of the invention, determination of the unique coding sequence identifies the nucleotide sequence at the SNP site and its location within the genome. Determination of the unique coding sequence is achieved by sequencing this sequence. Landegren et al. (USPN 4,988,617) do not teach a method involving a first set of oligonucleotides comprising a unique label, wherein the label is a unique coding sequence of nucleotides which is specific for a particular nucleotide at a particular SNP site. Indeed, the Examiner acknowledges that Landegren et al. (USPN 4,988,617) do not teach an embodiment wherein the label of said first oligonucleotide set is a unique coding sequence of nucleotides. See page 6, paragraph 3 of the Office Action. Moreover, it is also follows that USPN 4,988,617 fails to teach a method wherein the identity of a nucleotide at a SNP site is determined by sequencing a unique label which is specific for a particular nucleotide at a SNP site. That being the case, Landegren et al. do not teach at least two features of the instant claims and, therefore, fail to anticipate the instant invention.

In view of the clarifying amendments to the claims and the above arguments, the Examiner is respectfully requested to reconsider the validity of the rejection of the claims under 35 U.S.C. §102 and withdraw the rejection.

Rejection Under 35 U.S.C. § 103

Claims 4 and 16-17 are rejected under 35 U.S.C. §103 (a) as allegedly unpatentable over Landegren et al. (USPN 4,988,617) as applied against claim 1 and further in view of Landegren et al. [US 2005/0287526 (2005)]. Claims 16-17 are canceled herein, thereby obviating any rejection of these claims. In view of the clarifying amendments to the claims and Applicant's arguments presented herein, the rejection as it applied to claims 4 and 16-17 is respectfully traversed.

As described herein above, the instant claims are drawn to a method that calls for a unique label, which is a unique coding sequence of nucleotides that is specific for the nucleotide complementary to the known SNP site and the position of the SNP to be scored. The Landegren et al. patent (USPN 4,988,617) fails to teach a unique label which is a unique coding sequence of nucleotides and, in turn, fails to teach a sequencing step wherein the unique label is determined. As indicated above, determination of the unique coding sequence identifies both the particular nucleotide at the SNP site and the location of the SNP in the genome. The Examiner recognizes that Landegren et al. (USPN 4,988,617) do not teach an embodiment wherein the label of said first oligonucleotide set is a unique coding sequence of nucleotides. Landegren et al. (US 2005/0287526) fails to remedy these deficiencies of Landegren et al. (USPN 4,988,617) with respect to the instant claims. Moreover, paragraph [0052] of Landegren et al. (US 2005/0287526), to which the Examiner refers, describes hairpin-forming probes wherein the diagnostic base is part of the hairpin forming sequence. As detailed therein, this configuration favours ligation of matched probes over misligation of mismatched probes. This configuration differs, however, from the present invention, wherein the hairpin probe does not comprise the SNP site. See, for example Figure 1.

In view of the above, Landegren et al. (USPN 4,988,617) and Landegren et al. (US 2005/0287526) do not, in combination, teach at least two features of the instant claims and, therefore, fail to render obvious the instant invention. In light of the above, Applicant also asserts that the Examiner has failed to meet the criteria required to establish a prima facie case of

obviousness. Reconsideration and withdrawal of this rejection of claims 4 and 16-17 is, therefore, respectfully requested.

Claims 5-6 and 18-19 are rejected under 35 U.S.C. §103 (a) as allegedly unpatentable over Landegren et al. (USPN 4,988,617) as applied against claim 1 and further in view of Brenner et al. (USPN 5,846,719; 1998). Claims 5-6 and 18-19 are canceled herein, thereby obviating any rejection of these claims.

Should this rejection be applied to the instant claims, however, Applicant asserts that the combined teachings of Landegren et al. (USPN 4,988,617) and Brenner et al. (USPN 5,846,719) would not lead a skilled practitioner to the instant invention. The Examiner acknowledges that Landegren et al. (USPN 4,988,617) do not teach an embodiment wherein the label of said first oligonucleotide set is a unique coding sequence of nucleotides. The Examiner relies on Brenner et al. for evidence that the use of oligonucleotide tags (i.e., a unique coding sequence of nucleotides) as well as labeled oligonucleotide tag complements was known prior to the instant invention. The disclosure of Brenner et al., however, fails to teach oligonucleotide tags comprising a unique coding sequence of nucleotides, wherein the unique coding sequence of nucleotides is specific for the nucleotide complementary to a known SNP site and the position of the SNP to be scored. Brenner et al. also fail to teach a sequencing step to determine the unique coding sequence of nucleotides, wherein such a determination identifies the nucleotide complementary to the known SNP site and the position of the SNP to be scored.

In contrast, Brenner et al. teach that each polynucleotide is tagged with a different tag and this step is achieved by using a repertoire of tags substantially greater than the population of polynucleotides. This is taught throughout the patent and the following passage at column 4, lines 34-59, for example, of Brenner et al. exemplifies this teaching:

> "The polynucleotides to be sorted each have an oligonucleotide tag attached, such that different polynucleotides have different tags. As explained more fully below, this condition is achieved by employing a repertoire of tags substantially greater than the population of polynucleotides and by taking a sufficiently small sample of tagged

polynucleotides from the full ensemble of tagged polynucleotides. After such sampling, when the populations of supports and polynucleotides are mixed under conditions which permit specific hybridization of the oligonucleotide tags with their respective complements, identical polynucleotides sort onto particular beads or regions. The sorted populations of polynucleotides can then be manipulated on the solid phase support by micro-biochemical techniques.

Generally, the method of my invention comprises the following steps: (a) attaching an oligonucleotide tag from a repertoire of tags to each molecule in a population of molecules (i) such that substantially all different molecules or different subpopulations of molecules in the population have different oligonucleotide tags attached and (ii) such that each oligonucleotide tag from the repertoire is selected from the same minimally cross-hybridizing set ; and (b) sorting the molecules of the population onto one or more solid phase supports by specifically hybridizing the oligonucleotide tags with their respective complements attached to such supports."

In other words, each polynucleotide is tagged indiscriminately, since a tag is attached to each polynucleotide. The presence of the attached tags is subsequently used to sort the polynucleotides via hybridization to sequences attached to a support that are complementary to each of the tags. There is no teaching or suggestion in Brenner et al. regarding a first set of oligonucleotides, each of which comprises a sequence of nucleotides that is complementary to a region on said genome that includes a known SNP site, wherein a nucleotide complementary to the known SNP site is at or near the 5' end of each of said oligonucleotides and each oligonucleotide further comprises a unique coding sequence of nucleotides, wherein the unique coding sequence of nucleotides is specific for the nucleotide complementary to a known SNP site and the position of the SNP to be scored. There is simply no particularity in the attachment of tags to polynucleotides in the method of Brenner et al. The unique coding sequences of Brenner et al. are <u>not</u> specific for a nucleotide complementary to a known SNP site and the position of the

SNP to be scored. The unique coding sequences of Brenner et al. do not, therefore, possess the recited properties of the unique coding sequences of the instant invention.

In light of the above deficiencies of Brenner et al., it is apparent that the combined teachings of Landegren et al. (USPN 4,988,617) and Brenner et al. (USPN 5,846,719) would not lead an ordinarily skilled practitioner to the present invention. It therefore follows that these references in combination do not support a potential rejection based on alleged obviousness and certainly fail to meet the criteria required to establish an alleged prima facie case of obviousness.

Claims 7 and 13 are rejected under 35 U.S.C. §103 (a) as allegedly unpatentable over Landegren et al. (USPN 4,988,617) as applied against claim 1 and further in view of Balasubramanian et al. (USPN 6,787,308; 2004). In view of the clarifying amendments to the claims and Applicant's arguments presented herein, the rejection as it applied to claims 7 and 13 is respectfully traversed.

The instant claims are drawn to a method that calls for a unique label, which is a unique coding sequence of nucleotides that is specific for the nucleotide complementary to the known SNP site and the position of the SNP to be scored. As described herein, Landegren et al. (USPN 4,988,617) fail to teach a unique label which is a unique coding sequence of nucleotides. This patent also fails to teach that determination of the unique label by sequencing serves to identify both the particular nucleotide at the SNP site and the location of the SNP in the genome. The Examiner recognizes that Landegren et al. (USPN 4,988,617) do not teach an embodiment wherein the label of said first oligonucleotide set is a unique coding sequence of nucleotides. Balasubramanian et al. (USPN 6,787,308) fail to remedy the above-indicated deficiencies of Landegren et al. (USPN 4,988,617) with respect to the instant claims. Indeed, the combined teachings of these references fail to provide any guidance relating to several recited features of the instant claims. In light of the above, Applicant asserts that the Examiner has failed to meet the criteria required to establish a prima facie case of obviousness. Reconsideration and withdrawal of this rejection of claims 7 and 13 is, therefore, respectfully requested.

Claim 20 is rejected under 35 U.S.C. §103 (a) as allegedly unpatentable over Landegren et al. (USPN 4,988,617) in view of Landegren et al. [US 2005/0287526 (2005)] as applied

against claim 4 and further in view of Brenner et al. (USPN 5,846,719; 1998). Claim 20 is canceled herein, thereby obviating any rejection of this claim.

In view of the amendments to the claims and arguments presented herein, the Examiner is respectfully requested to reconsider the validity of the rejection of the claims under 35 U.S.C. §103 and withdraw the rejection.

Fees

No additional fees are believed to be necessitated by this amendment. However, should this be an error, authorization is hereby given to charge Deposit Account No. 11-1153 for any underpayment or to credit any overpayment.

Conclusion

It is submitted, therefore, that the claims are in condition for allowance. No new matter has been introduced. From the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order, and such action is earnestly solicited. In the event that there are any questions concerning this amendment, or application in general, the Examiner is respectfully urged to telephone the undersigned so that prosecution of this application may be expedited.

Respectfully submitted,

Sarah J. Fashena

Sarah J. Fashena, Ph.D.
Agent for Applicant(s)
Registration No. 57,600

KLAUBER & JACKSON
411 Hackensack Avenue
Hackensack, New Jersey 07601
(201) 487-5800
August 6, 2007

Enclosures: Petition for a One-Month Extension of Time
Information Disclosure Statement